

OTS: 60-11,659

25
JPRS: 2688

20 May 1960

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- USSR -

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19981203 110

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RADIOACTIVE IODINE IN THE THERAPY OF THYROTOXICOSES¹

[This is a translation of an article written by K.D. Eristavi, T.O. Zhvaniya, N.N. Kebabze, and M.G. Gachicheladze of the Institute of Experimental and Clinical Surgery and Hematology, Academy of Sciences Georgian SSR, in Problemy Endokrinologii i Gormonoterapii (Problems of Endocrinology and Hormonotherapy), Vol VI, No 1, Moscow, 1960, pages 102-105.]

As early as the beginning of the twentieth century an attempt at treating exophthalmic goiter with radium was made by Abbe [14], after which a noticeable decrease of the volume of the goiter was observed. The cited observation served as the basis for the application to the thyroid gland of irradiation by X-rays with therapeutic purposes; however, this method of treatment did not find acceptance, because of frequent relapses of the disease and complications (carcinoma of the skin).

In connection with the selective adsorption of radioactive iodine by the thyroid gland and its destructive action, which was shown for the first time in the experiment of Hamilton and Lawrence [16], the prerequisites for study of the therapeutic action of radioactive iodine (¹³¹I) arose. Hertz [17] reported the successful clinical application of radioactive iodine in the treatment of several patients with thyrotoxicosis.

Radioactive iodine, concentrating primarily in the hyperfunctioning thyroid gland, subjects it to irradiation (beta rays) from within, which leads to the destruction and loss of a considerable part of the functioning thyroid follicles, as well as to a decrease of the functional activity of the thyroid gland. It was shown by means of histological investigations that under the influence of radiation the follicles of the thyroid gland lose their normal structure and are replaced by connective tissue.

Observations in the clinics of America, and later of Britain (1949) and France, confirmed the effectiveness of the new method of treatment of thyrotoxicoses with radioactive iodine. Foreign authors

¹Reported to the Scientific Council of the Institute on 29 December 1958.

[13, 15 and others] point out that application of I^{131} in doses to 15 millicuries in diffuse as well as in nodular goiter gives good result in the sense of complete removal of clinical symptoms of thyrotoxicosis in 86% of patients. As for complications, hypothyreosis of a temporary or chronic character was noted in 10% of the cases.

In 1954-1958, a number of works by domestic authors were published, in which were cited summary data (on 3500 patients) and personal clinical observations (on material from 20 to 216 patients) which apply to the therapeutic effect of application of radioactive iodine in patients with moderate and acute form of thyrotoxicosis [1, 2, 3, 4, 5, 6, 10, 9, 11, 8, 7, 12, and others].

The above enumerated authors note the appearance of an euthyroid condition (stable remission) from application of radioactive iodine in 70-90% of patients in diffuse goiter and in 50% of patients with presence of nodule in the struma [12]. The development of hypothyreosis, most often of a transitory character, took place in 10% under the method of single treatment and in 0.6% in the method of fractional introduction of I^{131} . In application of radioactive iodine with a therapeutic purpose in the course of 15 years abroad and 6 years in Soviet Union, the development of carcinomatosis was not noted. However, some foreign authors do not feel that this period of observation is sufficient for a final conclusion with respect to the risk of development of late carcinomatosis under the influence of I^{131} .

With respect to the recommended doses of I^{131} , there are various opinions in the literature. Some authors express doubts as to the expediency and effectiveness of the application of small doses [Atabek, A.A., and others]; others protest against the great impact of single and repeated doses of I^{131} [12].

The aim of our investigations is to study the effectiveness and expediency of the application of various methods of dosaging of I^{131} , to study the remote results of the treatment with I^{131} of thyrotoxicosis with diffuse and nodular goiter, which is important at the present time as well, as seen from the literature data cited above.

At the Institute of Experimental and Clinical Surgery and Hematology, Academy of Sciences USSR, from 1956 to 1958 inclusive, treatment with radioactive iodine was conducted on 46 patients with various form of thyrotoxicosis. Among the patients there were 38 females and 8 males. According to age group, the patients were divided as follows: 19-25 years 3 persons, 25-45 years 25 persons, 45-55 years 9 persons, and 55-77 years 9 persons.

The duration of the disease consisted of: 2 months to 1 year 15 persons, 1 year to 3 years 10 persons, 3 to 6 years 5 persons, 6 to 10 years 9 persons, 10 to 20 years 7 persons.

The degree and severity of thyrotoxicosis was determined on the basis of the complex of the clinical-laboratory data. Aside from the study of clinical peculiarities of patients, laboratory analysis of urine, blood, Wasserman reaction were performed; in some cases the

bilirubin content in blood basal metabolism according to Holden, were studied; Roentgenoscopy of thoracic cavity, electrocardiography, Roentgenokymography were performed. In all patients, as a rule, before and after treatment, the dynamics of the accumulation of radioactive iodine in the thyroid gland was studied.

The investigation of the functional condition of the thyroid gland by means of radioactive iodine showed that in 31 of 46 patients (70%) the function turned out to be increased - the percentage of inclusion of radioactive iodine consisted of 42 to 91%, and a rise of the curve was noted during the first 2-4 hours of investigation. In 12 persons the percentage of inclusion of radioactive iodine was within the limits of the upper normal limit or above - 31-38; in 3 of 46 patients it was normal - 14-27. During the first month after termination of I^{131} intake, high initial indexes of I^{131} of inclusion decreased insignificantly; still, the curve of I^{131} inclusion, characteristic for thyrotoxicosis, changed. Several months after treatment, in the presence of stable remission - a euthyroid condition - the percentage of I^{131} inclusion showed a fluctuation within the normal limits (14-27).

The above-cited data shows that the method of determination of thyroid gland function by means of radioactive iodine may fully reflect the true condition of the thyroid gland. V.M. Karatygin with co-workers and other authors prove that the given method of determination of the function of the thyroid gland by means of I^{131} is more accurate than the determination of basal metabolism according to Holden.

It should be noted that a high inclusion of I^{131} , aside from a favourable prognosis in the sense of therapeutic effect, gave a basis for selection of the necessary dose of I^{131} .

On the basis of the complex of clinical-laboratory data, in 8 patients a severe form was established; in 32 a medium, and in 6 a mild form of thyrotoxicosis.

Diffuse goiter took place in 34 patients, nodular and mixed in 6, thyrotoxic adenoma in 3, relapse of thyrotoxicosis after subtotal resection of the gland in 3 patients.

The increase of thyroid glands before treatment was as follows: Second-degree goiter in 18 persons, third degree in 19, fourth degree in 6 persons.

Before administration of a therapeutic dose of I^{131} , the patients as a rule terminated the intake of iodine preparations and bromide. Radioactive iodine in the form of a solution was ordered for the patients before breakfast in a mixture with 50 ml. of distilled water. To more seriously ill persons, the radioactive iodine was given under clinical conditions (15 persons); to the other 37 patients the treatment with radioactive iodine was conducted under ambulatory conditions. The dose of I^{131} in each separate case was determined from the individual peculiarities of the patient; with this, the duration and severity of the disease, age, size and condition of the thyroid gland as well as

the percentage of accumulation of I^{131} in it were taken into consideration.

In the beginning of observations in fractional dosage, the dose of I^{131} for a single dose was from 0.5 to 2 m curies; in a mild form of thyrotoxicosis we limited ourselves more frequently to a small single dose (2 m curies) or two doses of I^{131} (1-2 m curies). In a case of thyrotoxicosis of medium degree with a diffuse goiter, especially with nodular, these doses did not produce any effect; therefore we were forced to give them up and to go over to treatment with medium doses of I^{131} (3-4 m curies per intake) with subsequent repetition 2-3 times if there was any necessity for it. Thus, the total course dose was from 6 to 12-15 m curies. In 2 of 6 patients with a node in the thyroid gland, the total dose reached 22-46 m Cu. In the single method of dosage we did not use more than 6 m Cu. The time interval between intakes of I^{131} was determined during 5-6 days (biological period of half-life of I^{131}).

The repeated course of treatment was conducted not earlier than 2-3 months later. Before each administration of I^{131} , an analysis of patients' blood, urine was conducted; blood pressure was checked, as well as accumulation of I^{131} .

On 46 patients it was necessary to give for removal of symptoms of thyrotoxicosis: a single dose to 5 patients (2-4 m Cu), two doses to 10 (2-6 m Cu), three doses to 10 (6-10 m Cu), 4 and 5 times to 10 (6-12 m Cu), 5-10 times to 9 (12-22 m Cu) and 10 to 20 times to 2 patients (22-46 m Cu).

With respect to these patients, we have at our disposal remote data of observations over a period from 8 months to 2 years. Until now, all patients have been under dispensary observation. In the course of 1-2 weeks after intake of I^{131} the aggravation of all symptoms of thyrotoxicosis was frequently observed; a subfebrile temperature was also noted. 4-6 weeks after termination of treatment, sometimes later, a noticeable clinical improvement of the condition of patients took place. At earlier times, decrease of perspiration, general weakness, and irritability was noted; the sleep improved, temperature became normalized.

In a study of remote results up to 2 years after treatment with radioactive iodine, disappearance of basic symptoms of thyrotoxicosis or their considerable decrease is noted: tachycardia (pulse became normalized from 120-150 to 76 pulsations per minute), general weakness, tremor of extremities, perspiration. A considerable increase of weight was observed in patients, from 3 to 10 kilos; in several cases, 15-20 kilos.

A decrease of the size of the thyroid gland was found in 70% of all patients 4-5 weeks after intake of I^{131} . In cases with stable remission over a period of 10 months-1 year and longer, complete disappearance of goiter was observed. In decrease of symptoms of thyrotoxicosis in patients with a duration of the disease of 1-2 years, noticeable decrease of exophthalmos, disappearance of ocular symptoms

were noted. The majority of patients became capable of work. In 2 patients with medium severity of thyrotoxicosis, with absence of menstrual cycle and accompanying eczema of lower extremities (patient U), treatment with radioactive iodine on a background of stable remission (for the duration of 1 year) induced restoration of the menstrual cycle, disappearance of eczema, which took place during 20 years.

In several patients with a serious form of thyrotoxicosis with thyrocardiac manifestations, with arrhythmia and systolic murmur at the apex, under the influence of therapy with radioactive iodine normalization of pulse and its rhythm, occurred; murmur and other symptoms of thyrotoxicosis disappeared.

The study of the results of treatment with radioactive iodine in 46 patients with thyrotoxicosis (with the duration of observations from 6 months to 1 year in 22 patients, from 1-2 years in 24 patients) showed that in 23 patients cure occurred with complete disappearance of all symptoms of the disease; considerable improvement of the condition was observed in 13 persons; improvement in 7; in 4 patients with nodular goiter, toxic adenoma with accompanying parkinsonism, in severe thyrocardiac form with cachexia, there was no improvement.

No serious side effects in the process of treatment of patients were observed; in some cough was noted; in 2, manifestations of transitory hypothyreosis which disappeared after three days of taking thyroiodine. Leucopenia, which took place in several patients, had an unstable character, becoming normalized after intake of pentoxyl. In patients on whom several courses of treatment with I^{131} were conducted, aside from leucopenia, changes in leucocytic formula and thrombocytes were discovered.

CONCLUSIONS

1. If treatment of patients with thyrotoxicosis with radioactive iodine, does not replace, in some cases, radical surgical intervention, it is without doubt an effective conservative means of treatment in thyrotoxicoses of light degree as well as in medium and severe forms of the disease, especially in those cases when surgical treatment cannot be performed for various causes.

2. The study of a fractional method of dosaging I^{131} in small and medium doses showed good therapeutic effect in application of medium doses, the rationality of their repeated application (3-4 times) at intervals of 6 days, and the absence of therapeutic effect in application of small doses of I^{131} in patients with medium and serious forms of thyrotoxicosis.

3. The treatment with radioactive iodine may also be conducted ambulatorily under the following conditions: relapse of thyrotoxicosis after subtotal resection of thyroid gland, absence of effect in

medicinal therapy, refractivity and idiosyncrasy to iodine preparations and thyouracil; combination of thyrotoxicosis with other diseases (psychosis, liver disease, cardio-vascular insufficiency), refusal by patients of surgical therapy as well as in patients of advanced age, when surgical intervention is connected with the risk of the patient's life.

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Received 9 November 1959

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